CarePartners of Connecticut MEDICARE ADVANTAGE

Medical Necessity Guidelines

Medical Benefit Drugs

Breyanzi® (lisocabtagene maraleucel)

Effective: January 1, 2025

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	Yes ☒ No ☐

Applies to:

☒ CarePartners of Connecticut Medicare Advantage HMO plans, Fax 617-673-0956

☒ CarePartners of Connecticut Medicare Advantage PPO plans, Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Chimeric antigen receptor T-cell therapy (CAR-T cell therapy), a type of immunotherapy which may also be referred to as adoptive T-cell therapy, attempts to program patients' own immune systems to recognize and attack cancer cells. The first step in this therapy is to remove T-cells from the patient via apheresis, a process that removes blood from the body and removes one or more blood components (such as white blood cells, plasma, or platelets). The remaining blood is then returned to the body. The T-cells are then sent to a drug manufacturing facility or laboratory where they are genetically engineered to produce chimeric antigen receptors (CARs) on their surface. These CARs are what allow the T-cells to recognize an antigen on targeted tumor cells. The genetically modified T-cells are grown in the lab until there are enough of them (many millions) to freeze and return to the center treating the patient. There they are infused into the recipient with the expectation that the CAR T cells will recognize and kill cancerous cells that have the targeted antigen on their surface. Since the CART cells may remain in the body long after the infusion, it is possible the treatment can bring about long-term remission. CART cell therapy can be used to treat certain hematologic malignancies when the disease is relapsed or refractory to standard line(s) of treatment.

Food and Drug Administration (FDA) Approved Indications:

BREYANZI (lisocabtagene maraleucel) is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

- Adult patients with large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma, who have:
    - Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy
    - Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age
    - Relapsed or refractory disease after two or more lines of systemic therapy
- Adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have:
    - Received at least 2 prior lines of therapy including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor.
- Adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have received at least 2 prior lines of systemic therapy, including a Bruton tyrosine kinase (BTK) inhibitor.

Limitations of Use: Breyanzi is not indicated for the treatment of patients with primary central nervous system lymphoma.

REMS Program: Because of the serious risks of CRS and neurologic toxicities, BREYANZI is available only under a restricted program called BREYANZI REMS (Risk Evaluation Mitigation Strategy). The goals of BREYANZI REMS are to mitigate the risks of CRS and neurologic toxicities by:

- Ensuring that hospitals and associated clinics that dispense BREYANZI are specially certified and have on-site immediate access to tocilizumab.
- Ensuring that those who prescribe, dispense, or administer BREYANZI are aware of how to manage the risks of CRS and neurologic toxicities.

For more information about the BREYANZI REMS program, call 1-888-423-5436 or go to https://www.breyanzirems.com/.

Care Partners of Connecticut uses guidance from the Centers for Medicare and Medicaid Services (CMS) and MassHealth for coverage determinations for its Medicare Advantage plan members. CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and documentation included in the Medicare manuals are the basis for coverage determinations where available. For Care Partners of Connecticut members, the following criteria is used: Chimeric Antigen Receptor (CAR) T- cell Therapy NCD 110.24

Clinical Guideline Coverage Criteria

The Plan may cover Breyanzi for Members, when **all** the following criteria are met:

For Large B-cell lymphoma

1. The Member is 18 years of age or older and has been diagnosed with large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma

AND

2. Who have **one** of the following:
    a. Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy
    b. Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age
    c. Relapsed or refractory disease after two or more lines of systemic therapy

AND

3. The Member does not have primary central nervous system (CNS) lymphoma

AND

4. The treating facility is certified under the Risk Evaluation and Mitigation Strategy (REMS) System program for Breyanzi.

*****Relapsed/Refractory defined as disease progression after the last treatment regimen or refractory/suboptimal response to the most recent therapy

For Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic lymphoma (SLL)

1. The Member is 18 years of age or older and has been diagnosed with relapsed or refractory chronic lymphocytic leukemia (CLL) or Small Lymphocytic lymphoma (SLL)

AND

2. The Member has received two prior lines of therapy including a Burton tyrosine kinase (BTK) inhibitor (e.g. acalabrutinib, ibrutinib, zanubrutinib) and a B-cell lymphoma 2 (BCL-2) inhibitor (e.g. venetoclax).

AND

3. The treating facility is certified under the Risk Evaluation and Mitigation Strategy (REMS) System program for Breyanzi

Note: Documentation submitted must list previous lines of treatment/systemic therapies and date of each therapy.

For Mantle Cell Lymphoma

1. The Member is 18 years of age or older and has been diagnosed with relapsed or refractory MCL

AND

2. The Member has received two or more lines of systemic therapy including a Burton tyrosine kinase (BTK) inhibitor (e.g. acalabrutinib, ibrutinib, zanubrutinib) and a B-cell lymphoma 2 (BCL-1) inhibitor (e.g. venetoclax)

AND

3. The Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1.

In addition to the above criteria, the Plan may cover Breyanzi in an outpatient setting when all of the following criteria is met:

1. The provider attests that they have assessed the Member and determined that outpatient administration is clinically appropriate.

AND

2. The provider attests that the Member meets and understands the requirements of safety and monitoring post infusion as described by the Breyanzi REMS program[1].

Note: Prior authorization for Breyanzi is required regardless of hospital inpatient or outpatient setting.

ECOG Performance Status:

- 0: Fully active, no restrictions on activities. A performance status of 0 means no restrictions in the sense that someone is able to do *everything* they were able to do prior to their diagnosis.
- 1: Unable to do strenuous activities, but able to carry out light housework and sedentary activities. This status basically means you can't do heavy work but can do anything else.
- 2: Able to walk and manage self-care, but unable to work. Out of bed more than 50% of waking hours. In this category, people are usually unable to carry on any work activities, including light office work.
- 3: Confined to bed or a chair more than 50 percent of waking hours. Capable of limited self-care.
- 4: Completely disabled. Totally confined to a bed or chair. Unable to do any self-care.
- 5: Death

Limitations

- Members who have had prior treatment with any form of CAR-T cell therapy, including therapies in clinical trial settings, will not be approved for additional CAR-T therapy.
- Authorization for Breyanzi is limited to a one-time infusion
- All other indications other than those listed above are considered experimental/investigational and not medically necessary.
- Members cannot have Richter's transformation for the diagnosis of CLL/ SLL, as documented/suspected by rapid decline, or elevated levels of serum lactate dehydrogenase, and confirmed by biopsy

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
Q2054	Lisocabtagene maraleucel, up to 110 million autologous anti-CD19 CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic doses

Table 2: CPT Codes

CPT Codes	Description

References:

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3. United States Department of Health and Human Services, National Institutes of Health, National Cancer Institute. CAR-T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. Available at cancer.gov. Last accessed October 24, 2017.
4. Leukemia & Lymphoma Society. Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts. Available at lls.org. Last accessed October 20, 2017.
5. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2020;382(14):1331-1342. doi:10.1056/NEJMoa1914347.
6. Initial treatment of mantle cell lymphoma. UpToDate.com/login [via subscription only]. Accessed: July 30, 2020.
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8. Abramson JS, Palomba ML, et. al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicenter seamless design study. Lancet. 2020 Sep 19;396(10254):839-852. doi: 10.1016/S0140-6736(20)31366-0. Epub 2020 Sep 1. PMID: 32888407.
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nccn.org/professionals/physician_gls/pdf/b-cell_blocks.pdf. Accessed July 9, 2021.
12. Shah BD, Ghobadi A, Oluwole OO, et al. KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukemia: phase 2 results of the single-arm, open-label, multicenter ZUMA-3 study. Lancet. 2021;398(10299):491-502. doi:10.1016/S0140-6736(21)01222-8
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16. Siddiqi T, Maloney DG, Kenderian SS, et al. Lisocabtagene maraleucel in chronic lymphocytic leukaemia and small lymphocytic lymphoma (TRANSCEND CLL 004): a multicentre, open-label, single-arm, phase 1-2 study. Lancet. 2023;402(10402):641-654. doi:10.1016/S0140-6736(23)01052-8

Approval And Revision History

September 21, 2022: Reviewed by the Medical Policy Approval Committee (MPAC)

Subsequent endorsement date(s) and changes made:
- Originally approved at September 21, 2022 MPAC effective January 1, 2023
- Administrative update: November 2023 added Medical Benefit Drugs to title, updated CPCT logo, and clarified NCD language effective January 1, 2024
- October 18, 2023: Reviewed by MPAC, renewed without changes effective January 1, 2024
- December 1, 2023: Reviewed by the Joint Medical Policy and Health care Services Utilization Management Committee effective January 1, 2024.
- January 2024: added criteria for allow for outpatient administration and updated references effective March 1, 2024
- April 19, 2024: criteria updates reviewed and approved by the Joint Medical Policy and Health care Services Utilization Management Committee
- April 17, 2024: Reviewed at Medical Policy Approval Committee Added Indication for relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) effective June 1, 2024.
- July 22, 2024 Reviewed by MPAC added Mantle Cell Lymphoma indication and opened up to all Follicular Lymphoma, not just Follicular Lymphoma grade 3B, effective September 1, 2024. Added ECOG Table.
- November 21, 2024: Reviewed by MPAC, renewed without changes. Effective January 1, 2025.
- December 13, 2024: Reviewed by UM Committee; Coding updated: Removal of prior authorization from 0537T, 0538T, 0539T, and 0540T. Effective January 1, 2025.
- December 18, 2024: Reviewed by MPAC; Coding updated: Removal of prior authorization from 0537T, 0538T, 0539T, and 0540T. Effective January 1, 2025

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member's benefit document, and in coordination with the Member's physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.